General

Guideline Title

Non-small cell lung cancer stage III.

Bibliographic Source(s)

Alberta Provincial Thoracic Tumour Team. Non-small cell lung cancer stage III. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2012 Apr. 13 p. (Clinical practice guideline; no. LU-003). [36 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

1. Whenever possible, patients should be considered for eligibility in ongoing clinical trials.

Treatment for Operable Disease (T3N1, Selected T4N0-1)

2. Surgical resection is recommended.
3. Extended pulmonary resection may be performed in selected lesions. These include peripheral lesions invading the chest wall, apical lung carcinomas, central lesions with limited mediastinal invasion, or focal pericardial or phrenic nerve invasion. Carinal tumours and those within 2 cm of the carina occasionally may be amenable to resection with airway reconstruction.
4. Platinum-based chemotherapy regimens are recommended as post-operative adjuvant therapy in the management of patients with completely resected stage IIIA non-small cell lung cancer (NSCLC).
    - Cisplatin-based treatment is preferred, although carboplatin-based regimens can be used as an alternative if there is a contraindication to cisplatin.
5. Adjuvant radiotherapy after surgical resection is not routinely recommended. However, this treatment could be considered when there is microscopic involvement of the resection margin, including the bronchial resection margin.

Curative Intent Treatment for Inoperable Disease

6. Combined concurrent chemo-radiation is recommended for inoperable stage III patients with good performance status (Eastern Cooperative Oncology Group [ECOG] 0-2), minimal weight loss, good pulmonary reserve, and tumour and anatomy conformation permitting radical dose radiation without expected severe normal tissue toxicity.
    - Cisplatin-based chemotherapy (with either etoposide or vinorelbine) and thoracic radiation of 55 greys (Gy) in 25 fractions to 66 Gy

in 33 fractions is the recommended treatment option.

7. For patients with borderline performance status or moderate weight loss (5%-10%), concurrent or sequential chemo-radiation or higher dose hypofractionated radiation are options.

Treatment for T1-3N2 Disease

8. Concurrent chemo-radiation is recommended for pre-operatively diagnosed N2 disease. Cisplatin-based chemotherapy (with either etoposide or vinorelbine) and thoracic radiation of 55 Gy in 25 fractions to 66 Gy in 33 fractions is the recommended treatment option. Additional cycles of chemotherapy can be considered for bulky disease.
9. In select patients, neoadjuvant chemoradiotherapy followed by lobectomy can be considered. Pre-operative pathologically diagnosed N2 disease is not recommended to undergo surgical resection alone.
10. For patients with N2 disease discovered intra-operatively where complete resection of the lymph nodes and primary tumour is technically possible, completion of the planned lung resection is recommended.
11. In patients with N2 disease discovered intra-operatively, platinum-based adjuvant chemotherapy is recommended. Adjuvant radiotherapy can be considered in select patients.

Palliative Treatment for Inoperable Disease

12. In patients where lung reserve precludes radical radiotherapy, palliative chemotherapy and/or palliative radiotherapy are recommended.
13. Palliative chemotherapy options include:
    - 1st line: platinum-based doublets
    - 2nd line: docetaxel, erlotinib, or pemetrexed
14. For symptomatic patients with poor performance status (ECOG >2) and/or significant weight loss (usually defined as >10% in previous 3 months), radiotherapy for symptom palliation is recommended. Dose-fractionation schedule options include:
    - 20 Gy in 5 fractions or 30 Gy in 10 fractions
    - Single fractions of radiotherapy less than 10 Gy may be appropriate in some clinical circumstances such as poor performance status or patient travel distance.
    - Split course radiation can also be used in select cases.

For more information, please see the National Guideline Clearinghouse (NGC) summary of the Alberta Health Services guideline Non-Small Cell Lung Cancer Stage IV.

Follow up and Surveillance

15. Although there is no high level evidence, expert opinion recommends that a computed tomography (CT) scan be administered 3-6 months post-treatment.
16. Follow-up appointments are recommended every 6 months for the next 2 years. Chest x-ray or CT can be used for scans following the first appointment.

Clinical Algorithm(s)

A treatment algorithm is provided in the original guideline document.

Scope

Disease/Condition(s)

Stage III non-small cell lung cancer (NSCLC)

Guideline Category

Management

Treatment

Clinical Specialty

Oncology

Pathology

Pulmonary Medicine

Radiation Oncology

Radiology

Surgery

Thoracic Surgery

Intended Users

Physicians

Guideline Objective(s)

To provide consensus-based guidelines on treatment and management of stage III non-small cell lung cancer

Target Population

Adult patients over the age of 18 years with stage III non-small cell lung cancer

Interventions and Practices Considered

1. Considering patients for clinical trials
2. Surgical resection
3. Adjuvant postoperative chemotherapy (cisplatin- or carboplatin-based regimen)
4. Adjuvant radiotherapy (not routinely recommended)
5. Combined concurrent chemo-radiation for inoperable patients
6. Neoadjuvant chemoradiotherapy followed by lobectomy
7. Palliative treatment for inoperable disease
    - Palliative chemotherapy
    - Palliative radiotherapy
8. Follow-up and surveillance (chest x-ray or computed tomography scan)

Major Outcomes Considered

- 1-year, 2-year, 5-year, 7-year, disease-free, progression-free, and overall survival
- Tumour response rate
- Mediastinal complete pathological response
- Adverse effects and toxicity of treatment
- Treatment-related deaths

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Questions

1. What are the recommended treatment options for patients with operable stage III non-small cell lung cancer?
2. What are the recommended treatment options with curative intent for patients with inoperable stage III non-small cell lung cancer?
3. When is palliation recommended, and what are the recommended palliative treatment options for patients with inoperable stage III non-small cell lung cancer?

Search Strategy

For this guideline update, the working group conducted a search for new or updated practice guidelines published since September 2009 by accessing the websites of the following organizations: Cancer Care Ontario, the British Columbia Cancer Agency, Cancer Care Nova Scotia, the National Comprehensive Cancer Network, the American Society of Clinical Oncology, the Scottish Intercollegiate Guidelines Network, the National Institute for Health and Clinical Excellence, the American College of Chest Physicians, the European Society of Medical Oncology, Irish Journal of Oncology and Cancer Council Australia.

Medical journal articles were searched using the Medline, Cochrane Database of Systemic Reviews, and PubMed electronic databases. The search term "non small cell lung cancer stage III" was searched, including related terms. Limits placed on the search included: publication between 2008 and present, "meta-analysis", "clinical trial", "randomized controlled trial", "clinical trial, phase III", "clinical trial, phase IV", "controlled clinical trial", "humans", and "English". Results were further excluded if they were phase I or II clinical trials, included less than 100 patients with stage III non-small cell lung cancer (in clinical trials), were not related to treatment, focused only on the treatment of metastases, did not include an analysis of outcomes achieved by patients with stage III disease and did not discuss survival. The reference lists of relevant Cochrane reviews and guidelines by the American College of Chest Physicians (ACCP) and the National Comprehensive Cancer Network (NCCN) were scanned to further identify relevant phase III clinical trials.

The working group reviewed the acceptability and findings of all relevant literature and updated the guideline for the treatment of stage III non-small cell lung cancer. A draft of the guideline was then circulated to the entire provincial tumour team for final feedback and approval.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Thoracic Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

The working group reviewed the acceptability and findings of all relevant literature and updated the guideline for the treatment of stage III non-small cell lung cancer.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This guideline was reviewed and endorsed by the Alberta Provincial Thoracic Tumour Team.

When the draft guideline document is completed, revised, and reviewed by the Knowledge Management Specialist and the working group members, it will be sent to all members of the Provincial Tumour Team for review and comment. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with stage III non-small cell lung cancer

Potential Harms

Adverse effects and toxicity of treatment, including treatment-related deaths

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Thoracic Tumour Team and represents a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of Alberta Health Services, Cancer Care.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Alberta Provincial Thoracic Tumour Team. Non-small cell lung cancer stage III. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2012 Apr. 13 p. (Clinical practice guideline; no. LU-003). [36 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Apr

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

Alberta Health Services, Cancer Care

Guideline Committee

Alberta Provincial Thoracic Tumour Team

Composition of Group That Authored the Guideline

Not stated

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Thoracic Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. Alberta Health Services, Cancer Care recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Thoracic Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): Alberta Health Services, Cancer Care; 2011 Dec. 5 p. Electronic copies: Available in Portable Document Format (PDF) from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on December 20, 2012. The information was verified by the guideline developer on February 5, 2013. This summary was updated by ECRI Institute on July 18, 2014 following the U.S. Food and Drug Administration advisory on Docetaxel.

Copyright Statement

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